Optimising Patient Outcomes in Advanced **Gastrointestinal Stromal Tumours (GIST)** in Europe

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Introduction

GIST are malignant mesenchymal tumours and the most common sarcoma of the GI tract.[1]

KIT and *PDGFRA* mutations are the drivers of approximately 85% of GISTs.[2]

The standard of care for advanced GIST is treatment with TKIs.[1]

Progression through multiple lines of therapy is associated with deterioration in the QoL of patients with GIST, including cognitive and social functioning.[3]

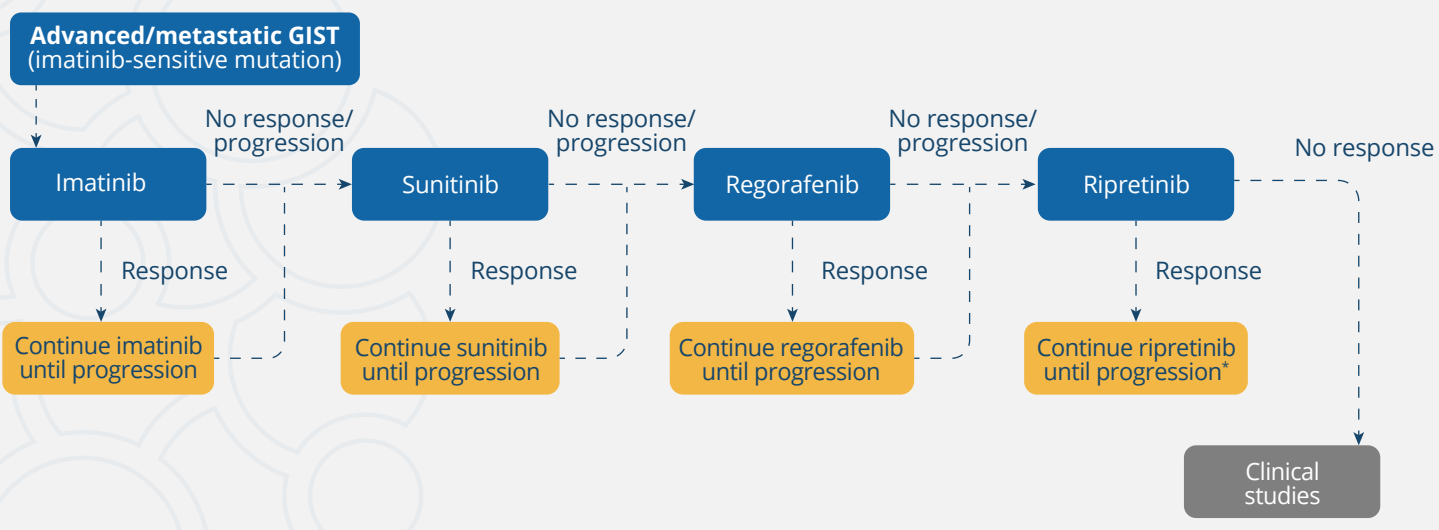
In advanced GIST, the treatment goals are to control disease progression and patient QoL.[1,3-6]

ESMO Guidelines Recommend Life-long Systemic TKI Therapies for Advanced GIST[1]

(ESMO–EURACAN-GENTURIS guidelines)[1]

The introduction of TKIs has revolutionized the treatment of GISTs, resulting in a substantial gain in median overall survival.[6]

Discontinuing TKI therapy can lead to accelerated disease progression or worsen symptoms.[1,4] Proactive adverse effect management is critical to ensuring patients continue on TKI therapy as appropriate.[4,7]



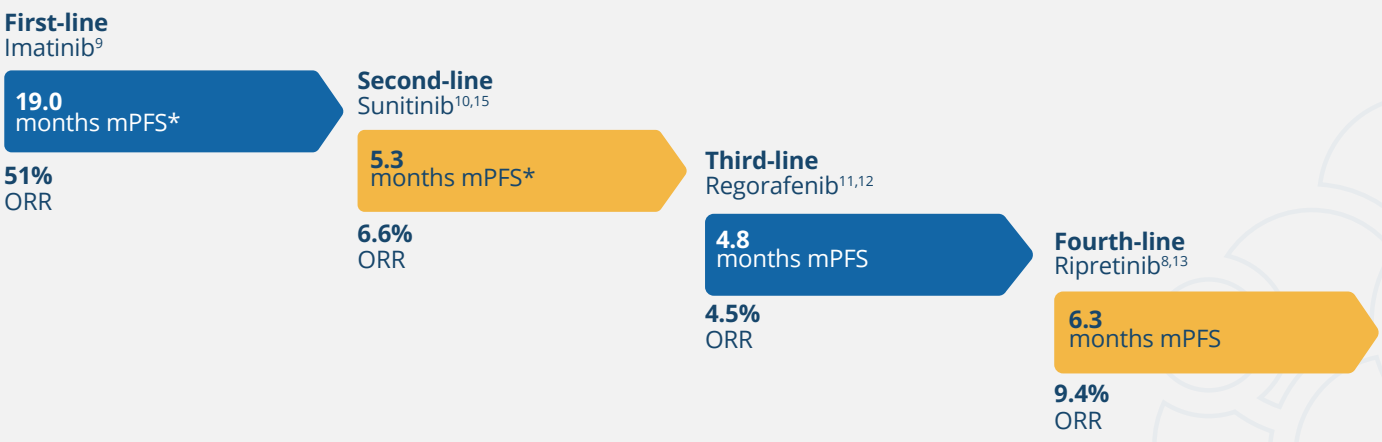
Avapritinib is indicated as monotherapy for the treatment of adult patients with unresectable or metastatic GIST harbouring the PDGFRA D842V mutation[1]

*Rechallenge with imatinib (to which the patient has already been exposed with evidence of response) or continuation of treatment beyond progression is an option[1]

Figure adapted from Casali PG et al. 2022.

TKI therapy improves patient outcomes in advanced GIST[8-15]

In advanced GIST, the ESMO guidelines recommend that treatment should be continued indefinitely where possible.[1] Toxicity management and tolerability during long-term treatment can be a challenge for some patients as severe and/or unmanaged toxicities may impact QoL and can lead to a lack of compliance, treatment interruption or treatment discontinuation.[1,7] Supportive measures, including proactive counselling, to manage toxicity are needed.[1]



Reported adverse reactions (very common events [≥1/10])

Imatinib	Sunitinib	Regorafenib	Ripretinib
Abdominal pain, anaemia, dermatitis/eczema/rash, diarrhoea, dyspepsia, fatigue, fluid retention/oedema, headache, muscle spasm and cramps, musculoskeletal pain, nausea, neutropenia, periorbital oedema, thrombocytopenia, vomiting, weight increased[14]	Abdominal pain, anaemia, arthralgia, back pain, constipation, cough, decreased appetite, diarrhoea, dizziness, dry skin, dyspepsia, dyspnoea, epistaxis, fatigue, hair colour changes, headache, hypertension, hypothyroidism, insomnia, leukopenia, mucosal inflammation, nausea, neutropenia, oedema, pain in extremity, PPES, pyrexia, rash, skin discolouration, stomatitis, taste disturbance, thrombocytopenia, vomiting[10,15]	Anaemia, asthenia/fatigue, constipation, decreased appetite and food intake, diarrhoea, dysphonia, fever, haemorrhage, hand-foot skin reaction, hyperbilirubinaemia, hypertension, increase in transaminases, infection, mucosal inflammation, nausea, pain, rash, stomatitis, thrombocytopenia, vomiting, weight loss[11]	Alopecia, arthralgia, back pain, blood bilirubin increased, constipation, diarrhoea, dry skin, dyspnoea, cough, fatigue, headache, hypertension, hypophosphataemia, lipase increased, muscle spasms, myalgia, nausea, oedema peripheral, pain in extremity, PPES, pruritus, seborrhoeic keratosis, vomiting, weight decreased[8]

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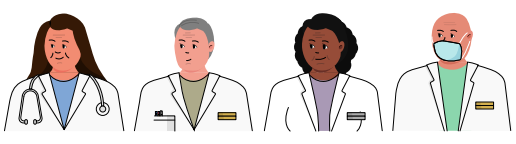
*PFS converted from weeks to months for sunitinib, and from years to months for imatinib

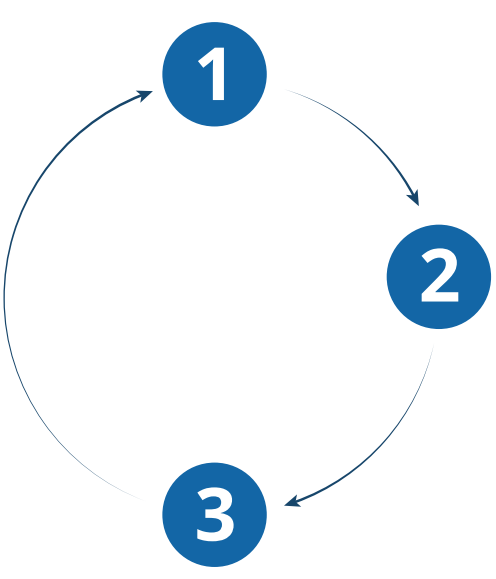
In Advanced GIST, Controlling the Disease Progression is Key

Interruption of TKI therapy may cause increased tumour activity and **rapid tumour progression**.[1,16]

Treatment management and change of lines of treatment should be evaluated **balancing radiologic progression and clinical benefit**.[1]



Management should be carried out at reference centres for sarcomas and GISTs and/or within reference networks utilising **multidisciplinary treatment planning**.[1]



1 Considerations when switching therapy[1,7]

Check in with patients often to monitor signs of progression or poor tolerability of current therapy, in line with ESMO guidelines

2 Reinforce treatment adherence[1,7,17]

Educating patients on risks and potential side effects prior to therapy initiation may facilitate adherence to TKI therapy

Strategies for managing side effects include supportive care, dose modifications, and treatment holds or discontinuations

3 Provide patients the opportunity to ask questions[7]

Facilitating increased communication prior to the start of therapy may enable early management of side effects

Conclusions

In advanced GIST, goals of care focus on controlling disease progression and patient QoL.[1,3,4,6]

ESMO guidelines recommend life-long systemic TKI therapies for advanced GIST, in order to improve patient outcomes.[1]

Consistent patient follow-up to monitor for signs of progression or poor tolerability of current therapy is recommended.[1] Patients progressing on or intolerant to current line of therapy should be considered for a change in treatment option.[1]

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Abbreviations:

ESMO: European Society for Medical Oncology; EURACAN: European Reference Network for Rare Adult Solid Cancers; GENTURIS: European Reference Network for Genetic Tumour Risk Syndromes; GI: gastrointestinal; GIST: gastrointestinal stromal tumour; mPFS: modified progression-free survival; ORR: objective response rate; PFS: progression-free survival; PPES: palmar-plantar erythrodysaesthesia syndrome; QoL: quality of life; TKI: tyrosine kinase inhibitor.

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